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Overview

Marijuana is an intoxicant. It's intoxicating effects are dependent on many factors, including the potency of the drug, the dose, the duration of use, the time since last use, the user's expectation of effects, the setting of use, the route of administration, and its consumption with other drugs, including alcohol. The impairing effects of the drug on complex task performance such as driving are similarly subject to many factors, making definitive statements about a subject's intoxication difficult, absent some objective observation of its well known and distinctive effects in the individual.

There is plentiful evidence that even moderate use of marijuana has real effects on some of the skills necessary for safe driving. The effects are most intense shortly after smoking, and are similar to those experienced with low to moderate doses of alcohol. On the other hand there are some marked differences between alcohol and marijuana intoxication. The intoxicating effects following recreational marijuana use generally dissipate within 2-3 hours following the end of smoking, whereas the impairing effects of alcohol generally persist longer. Also, in side by side comparisons of alcohol and marijuana intoxication, marijuana users appear to be more aware of their impairment, and there is evidence that by force of will they can suppress the impairing effects of their marijuana use for brief periods and perform well in non-sustained tests of performance. They can even compensate for the effects of marijuana on their driving under controlled conditions. This is markedly different from behavior in alcohol impaired individuals.

In this chapter we will consider the empirical properties of marijuana that have led to its popularity as a recreational drug, and consider how these effects impact the skills necessary for safe driving. We will examine the extent to which a relationship has been established between marijuana use and risk of crash involvement; review how an individual's level of intoxication can be assessed; and review studies of actual driving performance by subjects administered marijuana.

Effects of Marijuana

As is covered elsewhere in this book, after alcohol, marijuana is the most popular recreational drug in North America. Its effects are largely predictable in type, but not in degree, although they do appear in a roughly dose dependant manner. The effects discussed below make a very convincing case for the *potential* for marijuana to impair driving, although as noted the extent to which that potential is realized in a given case will be related to many other factors.

Getting "high"

People variously use marijuana for its exhilarating, relaxing, hallucinogenic, antinausea and soporific effects.

Marijuana is most frequently smoked, and less frequently eaten in baked goods or drunk as an infusion. Cannabis products including marijuana, hashish and hashish oil can be ingested orally, in tea or baked into brownies. The effect profile from oral ingestion is much longer, taking longer for the drug to be absorbed, and for the active THC to be distributed. The drug is likely subject to enterohepatic cycling when orally ingested, further complicating its kinetics. Metabolite concentrations are often highly elevated. It is not uncommon for the acute effects to last for 24 hours following oral ingestion. Oral use is also more frequently associated with adverse effects, such as paranoia, panic, depression and irritability. Currently available tests of blood or urine will not allow discrimination of the route of administration.

Following smoking, marijuana effects appear within five to ten minutes. The lower grade effects are remarkably similar to those resulting from alcohol consumption; relaxation, social disinhibition, and talkativeness. This disinhibition leads to users perceiving the drug effects as being mildly stimulatory at low doses. Users report the experience as producing a general sense of well-being, which can rise to the level of exhilaration or euphoria. It is described as a blissful state of reverie, fantasy, free-flowing thought and clarity. The senses are heightened, with colors, smell, touch, taste, and body perception being enhanced. Cravings for food are common. Bouts of uncontrollable spontaneous laughter or giggling are regularly seen, with even common events appearing to be funny or amusing.

The perceptual effects of marijuana use have an association with driving impairment due at least in part to their distracting nature. The degree to which someone is absorbed in their drug experience will affect their inclination to engage fully in other demanding tasks such as driving. The degree of effect will differ from individual to individual and can be significantly affected by the setting.

Physiological effects

The physiological effects of marijuana use are more tenuously related to driving; however they are useful indicators in assessing a person for recent marijuana use. Delta-9-tetrahydrocanabinol (THC) is a vasodilator, and within minutes of smoking marijuana, peripheral vasodilation leads to a precipitous drop in blood pressure, and a reflex increase in heart rate. Users can feel dizzy or faint, until homeostasis is restored. The dilatory effects of the drug on the capillaries in the sclera produce a distinctive reddening of the eyes, giving them a bloodshot appearance. Users usually report a dry throat and mouth. Among the other effects on the eyes are loss of convergence or ability to cross; hippus (an intermittent change in the size of the pupil occurring without external stimuli); and rebound dilation following changing light conditions, where the pupil size will oscillate before stabilizing. Nystagmus, or the ability of the eye to track smoothly, is affected by marijuana, and becomes more prominent under conditions of very high or repeated dosing.

While these effects are not indicators of <u>impairment</u> *per se*, this characteristic set of symptoms can be relied upon by police officers or medical personnel to make a connection between an individuals appearance of intoxication and their recent marijuana use.

Cognitive and psychomotor effects

Driving is a complex task requiring the integration of various cognitive and psychomotor skills. Cognitive skills are those related to the processes of knowing, thinking, learning, and judging. For driving these effects include memory, perceptual skills, cognitive processing and task accuracy, reaction time, and sustained and divided attention.

Impairment of short term memory and learning impairment following marijuana use is probably the most frequently reported and validated behavioral effect of marijuana use, and one for which there is the most consistent evidence. The link between memory impairment and driving impairment is however is difficult to make convincingly. The strongest argument is the contribution of memory impairment to focus and selective attention. A clear recollection of recent events, contributes to organizational and planning ability, and promotes goal-directed behavior and action, allowing the subject to devote available cognitive capacity more efficiently to the driving task.

The user's perception is altered with respect to the passage of time which appears to pass more quickly relative to real time. Impairment in perception of speed and distance may be related to the time distortion. Laboratory studies have shown that cannabis users lose the perceptual ability to identify simple geometric figures within more complex patterns when intoxicated. Such perceptual changes can influence a person's normal driving behavior in a potentially unsafe way.

Simple tests of cognitive processing such as measures of associative ability (e.g. digit symbol substitution, and Stroop color word test) have been shown to be adversely affected by acute cannabis use resulting in greater numbers of errors. The effect when compared to moderate doses of alcohol however is small.

Reaction time effects are also present and are more significant at higher doses, but generally are small compared to those observed with moderate doses of alcohol. Impairment indicators are more prominent in complex rather than simple reaction time tests, and subjects tend to perform more slowly and make more errors.

Driving is a divided attention task, and as such, laboratory assessments of divided and sustained attention performance have been scrutinized for evidence of effects. These tests show consistently that the greater the demands on cognitive processing ability, the more complex the tasks, and the more tasks to be attended to, the poorer marijuana-dosed subjects performed. This has important implications for marijuana and driving impairment and explains the findings in some of the on-road driving studies discussed later.

Driving demands varying levels of attention, cognitive capacity and psychomotor ability, depending on factors such as weather, road conditions, vehicle condition, other road user behavior, lighting, city versus highway driving, and many others. The threshold demands of driver performance for satisfactory vehicle operation might be within the subjects ability under normal driving conditions, but where the demands change unexpectedly, or emergencies arise, or there is a confluence of demands occurring at once (merging traffic, signal failure, unfamiliar neighborhood, road construction, etc) the driver's ability becomes surpassed and errors arise that result in crashes or bring the driver to the attention of the police. Peak cognitive impairment effects are reported to occur roughly 40-60 minutes following smoking and typically last for about two to three hours.

Hallucinations

The effects noted on heightened awareness of colors, smell, touch and taste, can be enhanced to the point where they constitute hallucinations – perceptions of things or sensations which do not exist. Objects can appear to "melt" or to lose or change form. Synesthesias can occur where, for example, sound or music can trigger visual or olfactory sensations. In most marijuana users who do experience these, they are more correctly characterized as pseudohallucinations since the user is aware that the perception is unreal even while experiencing it. Nevertheless, hallucinations of any kind are distracting and absorbing, and when they occur will impair attention and focus.

Infrequently, flashbacks are reported where individuals will re-experience or vividly recall the experience of a previous marijuana "trip". This can be triggered by environmental cues, or by readministration of marijuana or some other psychoactive drug.

Other adverse reactions

While many of the effects discussed above have the potential to be detrimental to driving, the adverse affects considered here are those not sought by the recreational marijuana user (a "bad trip"). They are atypical, but can be related to the users underlying frame of mind or mood, and are most commonly reported by naïve users. These include dysphoria, fearfulness, extreme anxiety, mild paranoia, and panic. When this occurs, its relationship to impairment of driving is clear. Typically at higher doses or in naïve users, sedation or sleepiness becomes a significant factor, and presumably users already tired would be more susceptible to this effect.

Discussion

Based on the above considerations it is clear than in many respects, marijuana has the ability to produce effects - both sought-after and incidental – which can affect the balance of skills and abilities needed to drive safely. These effects can vary in magnitude, but frequently when compared to effects of moderate dosing with alcohol, (for example to the presumptive level for intoxication in many US states of 0.08g ethanol/100mL blood) the impairing effects are less severe, even after the use of typical,

user-preferred doses. Additionally, the consistent observation that the impairing effects of marijuana after moderate use will dissipate in 2-3 hours, limits the likelihood of police contact or crash involvement if the driver allows some time to pass between their use and driving. The related ability of marijuana users to recognize the drug effect and take a less risky course of action also contributes positively to harm reduction.

On balance, the empirical evidence suggests that impairment observed following recent marijuana use can very reasonably be ascribed to the drug. This is most likely when the drug use, if moderate, is within three hours of driving. Beyond this time frame however, light to moderate marijuana use under normal demands of driving does not consistently generate impairment in driving skills that would come to the attention of the police, or result in increased risk of crash involvement.

Evidence of Marijuana Intoxication

Diagnosis of marijuana use – Physiological and psychomotor effects.

According to the Drug Recognition Expert (DRE) evaluation matrix used by police officers, characteristic symptoms of marijuana use include a lack of horizontal or vertical gaze nystagmus, pupil size dilated to normal, a lack of pupillary convergence, pupils will be normally reactive to light. Pulse is usually elevated within the first few hours following use, and blood pressure is correspondingly elevated. Body temperature will typically be normal. Speech may be slow or slurred, and muscle tone will be normal. Other clues include stale breath, sometimes users will have flakes or residue of marijuana in the mouth or a green discoloration of the tongue. The taste buds may be elevated due to irritation from the hot smoke. The user's eyes will typically be bloodshot, due to the vasodilatory effects of THC on the capillaries of the sclera. The face may be similarly flushed, and subjects may be diaphoretic. Nystagmus is not typically present, although some studies do suggest an association between acute marijuana use and nystagmus.

Subjects may have short attention spans, express hunger (THC is an appetite stimulant), and may giggle or laugh. If acutely intoxicated, users may also seem dazed, disengaged, or unconcerned. Because of the short distribution half-life of THC, users may also appear to sober up or improve in their performance and coordination during the first hour or two they are in custody.

Field sobriety tests have been criticized for having been validated for alcohol, and not for other drugs. The tests however are considered tests of impairment, that is they are tests which a normal sober person can perform without much difficulty, but that a person impaired in their cognitive and psychomotor skills cannot. Any errors in the test therefore may be considered indicators of impairment irrespective of its cause. A careful validation of the tests for marijuana has recently been performed in forty subjects. Papafotiou et al [Papafotiou, 2004] evaluated the efficacy of the standardized field sobriety test (SFST) 3 test battery on marijuana smokers. They applied the three tests,

horizontal gaze nystagmus (HGN), walk and turn (WAT) and One Leg Stand (OLS) tests at 5, 55, and 105 minutes after smoking a placebo, 1.74%, or 2.93% THC content marijuana cigarette. The data are summarized in Table 1.

Table 1. Relationship between time after smoking, average blood THC concentration (ng/mL) and percentage of subjects considered impaired under standardized field sobriety tests. [Papafotiou et al, 2004].

	Time 1 (0)-5 mins)	Time 2(50-5:	5 mins) T	Time 3 (100-	·105 mins)
Dose	Blood	% impaired	Blood	%	Blood	%
	THC		THC	impaired	THC	impaired
Placebo	0	2.5%	0	7.5%	0	5%
1.74% THC	55.5	23%	6.8	23%	3.7	15%
2.93% THC	70.6	46%	6.2	41%	3.2	28%

The study showed both dose dependant increases in rates of impairment in the subjects, with the most pronounced effects closest to smoking. It also confirmed low rates of failure in the test 2.5 - 7.5% in non intoxicated subjects. After 100 minutes, symptoms of impairment were beginning to diminish. The authors also noted a fourth category of head movements and jerks (HMJ). Adding the HMJ observations improved the diagnostic value of the tests by between 5 and 20%, and should be considered for future inclusion in a battery of tests for drug impairment.

Individually, the walk and turn test elicited significant differences in performance between the marijuana and placebo conditions, but MHT (Misses Heel to Toe), IT (Improper Turn) and INS (Incorrect Number of Steps) appeared almost as often in the placebo session as they did in the THC conditions and are therefore likely to be observed irrespective of drug consumption. Balance, and ability to focus attention was impaired at all three time points. Of the three tests the One Leg Stand was the most significant at all three time points, with poorer performance being significantly related to the level of THC at all testing times, as was performance on all of the scored signs of this test, except for hopping at Time 3.

Overall, when impairment caused drugs including marijuana is present, it apparently can be detected by the tests currently in widespread use by police officers. It is likely that these tests can be further refined to increase their effectiveness and sensitivity.

Toxicological tests

Marijuana use can be demonstrated by a chemical or toxicological test. Toxicological tests for detection of marijuana use, currently include hair, urine, blood,

¹ Time 1 represents 0 minutes after smoking for blood sampling and 5 minutes for the SFSTs. Time 2 represents 50 minutes after smoking for blood sampling and 55 minutes for the SFSTs. Time 3 represents 100 minutes after smoking for blood sampling and 105 minutes for the SFSTs.

sweat, and oral fluid. Hair marijuana tests offer the possibility of looking at marijuana exposure over the time period during which the hair was growing. Hair grows at rate of about a centimeter a month, and most commercial vendors offering hair testing will test a 3cm (~3 month) section closest to the scalp. Upon request a longer length can be tested, in sections if necessary, to assess patterns of use over the lifetime of the growth of the hair. This test has little applicability in assessing intoxication at any particular point in time however, as would be relevant in an impaired driving investigation. If the subject's prior marijuana use became an issue however this approach may offer some qualitative insight.

Toxicological evidence - Urine

As discussed elsewhere in this book, THC is metabolized to 11-OH-THC, and 11carboxy-THC (THC-COOH). The latter compounds are glucuronidated and excreted in the urine. Substantial variation exists in the excretion patterns of marijuana metabolites in subjects' urine. THC metabolites appear in the urine in detectable amounts within 30-90 minutes following smoking, however they may not reach the levels needed to cause a positive response at typical thresholds used for screening. Many laboratories use the 50ng/mL screening cut-off mandated for federal workplace urine drug testing, however study of six subjects showed that first void urine specimens after smoking a single 3.55% THC marijuana cigarette quantitated below that threshold in five of six subjects, at times ranging from 1-4 hours (mean 3.0 hrs) [Huestis, Mitchell, Cone, 1996]. In the same subjects, each smoking an identical 3.55% THC cigarette, peak urine concentrations varied considerably (29-355ng/mL, mean 153ng/mL) as did the time to peak (5.6 - 28)hrs, mean 13.9 hrs). Similarly, urine specimens confirmed positive by GCMS at a 15ng/mL cut off for between 57 and 122 hours following this single use (mean 89 hours or 3.7 days). The same authors have reported similar results in other subjects [Huestis, Mitchell, Cone, 1995]. Using a lower threshold, for example 20ng/mL, was shown to be more effective in identifying use for a longer period of time, and presumably for earlier detection of use in urine samples.

Other workers have evaluated the time it took for urine samples to test consistently negative in chronic marijuana users [Ellis et al, 1985]. These authors identified an extreme case of a subject who took 77 days to produce ten consecutive negative urine samples, screened at a 20ng/mL cut-off. Of the 86 subjects evaluated, the mean time to the end of their consecutive positive results at that threshold was 27 days.

There are significant implications following from these and similar studies for the use of urine as the specimen in a DUID setting. A specimen taken up to three hours after smoking marijuana may test negative for cannabinoids, depending on the screening threshold used, and the potency of the marijuana smoked. This, even though the subject would have experienced the peak effect within a few minutes, and would have been under the influence of marijuana at the time of driving or arrest. Also, following single acute use by naive users, urine concentrations may peak, then drop below detectable levels over the space of a few hours. Conversely, the presence of marijuana metabolites

in a subject's urine may have resulted from drug use several days earlier, considerably after the impairing effects of the drug have passed.

In summary, a positive urine test for THC-COOH cannot be used to infer either intoxication, or marijuana use within any forensically useful time frame. At best, if coupled with objective observations of physiological signs and symptoms of marijuana use, and documentation of psychomotor impairment, it can substantiate an opinion that observed impairment was due to marijuana use.

Toxicological evidence - Blood

Blood or plasma² analysis of THC provides the most direct toxicological evidence of recent marijuana use, and consequently of intoxication. Here are several approaches to the interpretation of blood toxicological data.

THC and THC-COOH concentrations

Since the effects of marijuana use have a relatively rapid onset when smoked, users can titrate the effects against the rate of administration to maximize the desirable drug effects while minimizing the adverse effects. Various studies have attempted to identify a "user preferred" dose of marijuana. These have established a typical user preferred dose of about 300ug/Kg, or about 21mg in a 70Kg (154Lb) individual [Robbe and O'Hanlon, 1993]. In terms of what this translates to in marijuana cigarettes, that will depend on the THC content of the marijuana, and the individuals smoking technique, with more efficient absorption achieved with deeper inhalation and breath holding.

For context, a standard NIDA marijuana cigarette (weight 558mg) having 3.58% THC content would deliver 20mg of THC, although not all of that may be bioavailable, depending on the subjects smoking technique. Plasma concentrations of THC and THC-COOH from one study with different levels of dosing are shown in table 1.

Table 2. Mean, median and range of THC and THC-COOH concentrations in plasma of subjects (n=14) under various dosing conditions (Table 5.4 from Robbe and O'Hanlon, 1993)

		100ug/Kg		200ug/Kg		300ug/Kg	
		t=35	t=190	t=35	t=190	t=35	t=190
THC	Mean	7.9	0.7	12.0	1.0	16.1	1.5
(ng/mL)	Median	6.5	0.9	10.0	1.1	15.8	1.5
	Range	0.8 - 17.2	0.0 - 1.3	1.5 - 27.1	0.0 - 2.7	4.7 - 30.9	0.4 - 3.2

² Most pharmacokinetic studies have made measurements of THC and its metabolites in plasma, while in a forensic context whole blood is the most commonly analyzed specimen. The plasma to whole blood ratio for cannabinoids is approximately 2:1 [Owens et al, 1981; Skopp et al, 2002], therefore when comparing whole blood concentrations to plasma concentrations, the plasma concentrations should be divided by 2.

ТНССООН	Mean	8.2	4.1	12.2	7.61	15.3	10.0
(ng/mL)	Median	7.4	4.1	11.2	6.4	13.0	8.2
	Range	1.4 - 19.4	0.0 - 12.0	2.0 - 37.2	0.0 - 32.2	4.2 - 39.6	1.5 - 36.3

Current street marijuana strength can vary considerably, from essentially zero, to 20% THC content or more, consequently predicting THC concentration or impairment based on a history of how many "joints" were smoked is inadvisable.

Peak blood or plasma THC concentrations occur within a few minutes of the end of smoking, and begin a rapid decline as the drug distributes from the central compartment into tissues. There is widespread agreement that the peak effects of the drug occur after the blood concentration has peaked and begun to decline. Plasma THC concentrations of 2-3 ng/mL (equivalent to whole blood concentrations of 1-1.5ng/mL) were linked by several authors to recent use (within 6-8 hours), and consequently of potential impairment of some psychomotor functions [Barnett and Willette RE, 1989; Huestis, Henningfield and Cone, 1992; Mason and McBay, 1985]. Other authors have suggested that whole blood concentrations of 1.6ng/mL or greater may cause psychomotor effects.

Detection of THC-COOH in the absence of any detectable parent drug is a not infrequent finding in DUID cases. This emphasizes the importance of using appropriate cut-off's for confirmatory testing, which should be of the order of 1ng/mL or less for both THC and THC-COOH. Assuming those thresholds are observed, data such as that in table 1 and in other work suggests that even following acute impairing doses of marijuana, concentrations of THC are likely to have become undetectable within about three hours following use, while THC-COOH may persist longer. In chronic users, THC concentrations of 2ng/mL have been shown to persist for more than 12 hours.

These limitations highlight the importance of obtaining a timely blood sample when investigating cases of impaired driving attributed to marijuana use.

THC/THC-COOH ratio

As noted above, peak psychomotor and cognitive effects following marijuana use occur within the first hour after smoking, a time interval during which the THC concentration is falling rapidly, and THC-COOH is beginning to appear as a result of oxidative metabolism. Several studies [Robbe and O'Hanlon, 1993; Huestis, Mitchell Cone, 1996; Mason and McBay, 1985] suggest that following single acute administration, THC-COOH concentrations will surpass THC concentrations within 30 to 45 minutes following initiation of use (see for example the patterns in Table 1). Consequently, THC/THC-COOH ratios of greater than 1 suggest use within the prior hour, the period during which effects are likely to be greatest.

In practice in a DUI setting, the likelihood of obtaining a specimen during the hour following initiation of smoking is small, due to the time taken to investigate, assess, and obtain a sample from a subject.

Algorithms for predicting time of marijuana use based on both THC concentrations and the THC/THC-COOH ratio have been described [Peat, 1989; Huestis et al, 1992;]. While preliminary data suggest that these models are accurate in predicting a likely time interval for last use following single acute moderate doses, they have not been extensively evaluated in chronic users, and have not been evaluated with THC concentrations below 2ng/mL, precluding their use in many DUID cases. While these models may be informative for evaluation of cases, readers are urged to exercise caution in their application in a forensic setting, since their limitations are still debated [Bogusz, 1993]. More extensive evaluation of this approach in chronic users is promising and warrants further study.

In a report of a GCMS method for the simultaneous determination of THC and THC-COOH in serum [Moeller et al, 1992], then applied this method to serial samples from subjects smoking 300ug THC/Kg body weight, and to 212 forensic serum specimens including driving cases. The samples from the smoking study showed THC concentrations in serum had fallen below 5ng/mL (equivalent of 2.5ng/mL in blood) in 33% of subjects within 100 minutes, and in 92% of subjects within 160 minutes following smoking. The distribution of concentrations of THC and THC-COOH in the forensic cases are shown in table 2, and illustrate that delays between the time of driving and the time of sample collection can result in undetectable THC concentrations. 87% of these cases have blood equivalent THC concentrations less than 1.5ng/mL.

Table 3. Distribution of THC and THC-COOH concentrations in forensic serum specimens (n=212) [Moeller et al, 1992]. ***Note: The corresponding whole blood concentrations would be approximately half the reported serum amount.

(ng/mL)	< 0.5	0.5 - 3.0	3.0 - 5.0	5.0 - 7.0	7.0 - 9.0	>9.0
THC	32%	55%	9%	2%	2%	0.5%
THC-COOH	26%	42%	18%	8%	2%	4%

Toxicological evidence - Oral fluid (saliva)

Oral fluid (saliva) is receiving a lot of scrutiny for its efficacy in detecting marijuana usage at the time of driving. Oral fluid is a plasma ultrafiltrate produced through the parotid and other glands in the mouth. Many water soluble drugs appear in this ultrafiltrate and can be detected by on-site immunoassays. Due to its lipophilicity, THC does not readily transfer from the blood to the oral fluid, however contamination of the oral cavity during smoking, from the smoke and possibly from marijuana debris from the cigarette, can result in a positive test within 30-90 minutes of use.

Oral fluid testing is still somewhat controversial. Many of the devices currently being sold are not consistently reliable, subject to operator error, and not comprehensive in terms of the drugs they test for. Additionally, the role of roadside testing is still a

subject of debate. As the tests are not comprehensive, drivers who appear impaired should be arrested regardless of the results of the roadside test, making it somewhat superfluous. The presence of the drug must still be confirmed by forensically acceptable techniques, requiring re-sampling or preservation of the roadside sample, and subsequent laboratory tests.

Summary

Blood concentrations of both THC and THC-COOH drop precipitously in the first few hours following smoking, as these substances partition into fatty compartments. It is recommended that blood or plasma concentrations of THC and THC-COOH be interpreted with caution. Under most circumstances, detection of parent THC will reflect recent use, meaning within the last few hours, making the likelihood of impairment within that time frame that much greater. More distant, higher intensity marijuana use cannot be ruled out however when THC is detected, and under that pattern of use impairment may persist longer than the 2-3 hours typical of the low to moderate dose administration. Detection of THC-COOH in the absence of the parent drug (i.e.<2ng/mL) tends to suggest more distant use (greater than 2 hours). It should go without saying that the screening threshold and confirmatory test sensitivity of the analytical laboratory must be taken into consideration when evaluating these results.

Epidemiology of marijuana and driving

A thorough review of epidemiological studies related to marijuana in various driving populations was done recently by Huestis [Huestis, 2002], and we will not attempt to replicate that here. The focus of this discussion will be on studies that have attempted to relate marijuana use to risk of accident involvement or accident culpability.

A survey of many of the studies cited by Huestis show various rates of marijuana positivity in impaired drivers, fatally injured drivers, and drivers injured in motor vehicle accidents, and commercial vehicle operators. The rates of positivity vary depending on whether blood or urine was tested, whether the parent or metabolite was tested for, whether the samples were provided voluntarily or following arrest, the sensitivity of the testing method, and whether the study group was selected out (e.g. only subjects without alcohol were tested). In spite of these variables, overall in the fatally injured driving population, ten to twenty percent of drivers test positive for cannabinoids, while in the arrest population rates are between 15 and 60%, suggesting a significant role for marijuana use.

None of these studies has control data however, which would show the rate of marijuana use in the local driving population NOT killed or injured in a collision, such that a comparative rate, or odds ratio for fatal accident involvement could be calculated. Another limiting factor was that in some studies urine was tested, and as noted above, urine can test positive for marijuana use for a few days following use, while the impairing effects last only for a few hours.

These studies do uniformly find evidence however that there is widespread use of marijuana in all these driving populations. In non-selected populations, (e.g. all fatally injured drivers, trauma patients) the incidence of cannabinoid positives was typically between 5 and 20%, and in selected populations (e.g. young males, fatally injured drivers) the rate was as high as between 15 and 60%.

A recent voluntary test of commercial vehicle operators in Washington and Oregon [Couper et al, 2002] showed marijuana positive rate of 5%, in spite of a 19% refusal rate in what is a heavily regulated industry with mandatory random testing. A similar survey done in 1988 showed 15% of tractor trailer drivers positive for cannabinoids, suggesting some improvement following the introduction of testing [Lund, 1988].

Assessment of relative crash risk following marijuana use.

Studies that have assessed crash responsibility offer more insight to the quantitative relationship between marijuana usage and crash involvement. An excellent review of culpability studies has recently been published [Ramaekers et al, 2004] The general design of these studies is to compare rates of drug use in at fault drivers versus no-fault drivers, and compute the ratio, with values over 1.0 indicating increased rates of risk. The 95% confidence interval is also computed and when the range includes 1.0, the difference in responsibility rates is not significant at the p=0.05 level.

In most of these studies, authors validate their data set and methodology by assessing odds ratios for alcohol. The relationship between alcohol and risk of crash involvement has been well established most famously in the 1960 Grand Rapids Study. In each case the method showed the expected significant relationship at the p=0.05 (95% CI) level between alcohol positivity and greater odds of crash involvement.

Table 4. Summary of odds ratio (OR) of becoming involved in fatal or injurious traffic accidents under the influence of cannabis, alcohol or their combination as reported in culpability studies [Ramaekers et al, 2004].

Substance	Authors	Odds ratio	95% CI
Drug free cases		1.0	
Alcohol	Terhune and Fell (1982);	5.4*	2.8-10.5
	Williams et al. (1985);	5.0*	2.1-12.2
	Terhune et al. (1992);	5.7*	5.1-10.7
	Drummer (1994);	5.5*	3.2-9.6
	Hunter et al. (1998);	6.8*	4.3-11.1
	Lowenstein and Koziol-Mclain (2001);	3.2*	1.1-9.4
	Drummer et al. (2003b)	6.0*	4.0-9.1
тнс-соон	Terhune and Fell (1982);	2.1	0.7-6.6
	Williams et al. (1985);	0.2	0.2-1.5
	Terhune et al. (1992);	0.7	0.2-0.8
	Drummer (1994);	0.7	0.4-1.5
	Hunter et al. (1998);	0.9	0.6-1.4
	Lowenstein and Koziol-Mclain (2001)	1.1	0.5-2.4
THC (range: ng/ml)			
<1.0	Hunter et al. (1998)	0.35	0.02-2.1
1.10-2.0		0.51	0.2-1.4
>2		1.74	0.6-5.7
1-100	Drummer et al. (2003a,b)	2.7*	1.02-7.0
5-100		6.6*	1.5-28.0
Alcohol/THC or THC-COOH	Williams et al. (1985);	8.6*	3.1-26.9
	Terhune et al. (1992);	8.4*	2.1-72.1
	Drummer (1994);	5.3*	1.9-20.3
	Hunter et al. (1998);	11.5*	4.6-36.7
	Lowenstein and Koziol-Mclain (2001)	3.5*	1.2-11.4

Significant changes in OR is indicated as follows: *<0.05.

The data from studies which made odds ratio assessments based on the presence of the inactive THC-COOH metabolite uniformly failed to show significant differences at the p=0.05 level in rates of accident involvement for the drug positive drivers. This can be rationalized in terms of the fact that the metabolite is inactive, and that in most cases urine was being tested. Bearing this in mind, together with the fact that urine can test positive for the metabolite for many hours or even days after the effect has passed, its detection in urine is not a good surrogate for impairment, and the negative findings are not surprising.

Studies assessing crash risk based on parent THC in blood are more informative. One study of 2500 injured drivers [Hunter et al, 1998; Longo et al, 2000] showed a trend towards increasing odds ratio with increasing THC concentration (although not significant at p=0.05), and found that culpable drivers had a higher mean THC concentration (p=0.057). This suggests a dose dependant increase in risk, with the threshold for significance being somewhere above 2ng/mL THC. One limitation of the Hunter study is the lack of control of the interval between driving and when the sample was collected. Intervals of an hour or less between the driving and the time the sample was collected would cause appreciable decreases in THC concentration.

In a cohort of 3398 fatally injured drivers [Drummer et al, 2004] the authors avoid this limitation since absorption of THC will stop at the time of death. That data shows an odds ratio of 2.7 in cases in which THC was detected, and 6.6 when the THC concentration was greater than 5ng/mL.

Several studies have evaluated crash risk in drivers positive for both alcohol and marijuana (THC or THC-COOH). Table 4 shows that irrespective of whether the parent drug or metabolite was measured, when combined with alcohol the odds ratio for crash involvement was between 3.5 and 11.5 (significant in all cases, p=0.05), and compared to alcohol positive cases was still significant with an odds ratio of 2.9.

Taken together this data represents strong evidence for a concentration (and consequently dose) dependant relationship between THC and risk of crash involvement, and enhanced risk for any use of marijuana when combined with alcohol.

Marijuana and on-road driving studies

The above considerations suggest that in addition to the empirical intoxicating properties of marijuana, there is epidemiological and behavioral evidence that it can cause impairment in the first few hours following use. Assessments of psychomotor performance following marijuana use have been performed and these have been reviewed recently by Ramaekers et al [Ramaekers et al, 2004]. These studies support that dose dependant impairment in psychomotor performance and cognition appear immediately following marijuana administration, peak after the blood concentration peaks, and persist for 3-4 hours. While there is a relationship between many of these tasks and the driving task, the clearest means of assessing the actual effects of marijuana on drivers is to measure their performance in actual on road driving following marijuana administration. A number of such studies have been done.

Klonoff et al., 1974

Conducted in Vancouver BC in the early 1970's, drivers were dosed with 4.9mg or 8.4mg of THC by smoking. This represents 70 and 120ug/Kg respectively in a 70Kg person, compared to 300ug/Kg described by Robbe and O'Hanlon as the user preferred dose, so both should be considered relatively low dose conditions compared to normal patterns of use. Following drug administration, drivers drove both on a closed traffic free course and on the streets of downtown Vancouver during peak traffic hours.

Driving performance was rated subjectively by a professional driving examiner. Researchers found subtle differences between the marijuana and placebo conditions, and noted some bidirectional changes in performance. Sixty four volunteers drove the driving course. There was a trend towards a greater number of subjects demonstrating poorer performance going from placebo, to low to high dose, with 73% of the high dose subjects demonstrating a decline in performance. However, 23% of subjects demonstrated an increase in performance in the high dose condition, with 14% showing significant improvement.

Thirty eight subjects participated in the on-street driving. Similarly while 79% of subjects demonstrated a decline in driving performance, 16% demonstrated improved performance even in the high dose condition.

The components of driving that were most affected by marijuana following the high dose were judgment, care while driving, and concentration. Minimally affected were factors such as general driving ability, speed, confidence, and aggression, and cooperation and attitude were unaffected. Unusual behaviors documented in drivers after marijuana use included missing traffic lights or stop signs, passing without sufficient caution, poor anticipation or handling of the vehicle with respect to traffic flow, inappropriate awareness of pedestrians or stationary vehicles, and preoccupation and lack of response at green lights.

While the tendency was towards deterioration in driving performance with increasing dose of marijuana, the trend was not uniform. The authors struggled to explain the bidirectional changes in performance, and hypothesize that inter-individual differences in response can outweigh dose related effects, and that subjects can recognize impairment and compensate, and in some cases overcompensate, resulting in improvement.

Caution should be exercised in applying the results of this study to users engaging in more demanding driving, and also to drivers using higher doses and more potent marijuana.

Robbe and O'Hanlon, 1993

The most comprehensive work on marijuana in actual on road driving has been done at the University of Maastricht in the Netherlands, beginning with this report. The authors first made an assessment of what dose of marijuana is preferred by users, so that appropriate doses could the assessed for their effects on driving. Twenty four subjects who sued the drug more than once a month and less than daily, and who had driven within an hour of marijuana use within the last year were assessed. Their average preferred dose in order to achieve the desired psychological effect was 20.8mg, which was after adjustment for body weight was 308ug/Kg, with no significant difference for males and females.

Subjects were tested on a closed driving course with doses of 0, 100, 200 and 300ug/Kg THC. Interestingly 40-60% of the subjects indicated they would have been willing to drive for unimportant reasons shortly after smoking the two highest doses. Driver

performance was assessed by measurement of standard deviation of lateral position (SDLP) an index of weaving which has been validated for alcohol and other drugs as a measurement of deterioration of driving performance.

There was dose dependant deterioration in SDLP. Driving performance decrement persisted undiminished for two hours following drug administration, even after perceived "high", and heart rate had declined. It also persisted even as measured plasma THC concentrations fell, however SDLP was not quantitatively related to plasma THC or THC-COOH concentrations. Drivers accurately assessed their performance as being poorer than normal under the two highest dose conditions. Quantitatively the decrement in SDLP was equivalent to blood alcohol concentrations (BACs) of 0.03-0.07g/100mL.

Having determined the scale of the performance decrement, the researchers decided it was safe to evaluate driving performance on open highways, around other vehicles under the same dosing conditions. Subjects were again dosed with 0, 100, 200 and 300ug/Kg THC. SDLP as an index of weaving, and a car following test where the subjects had to maintain headway with a lead vehicle were conducted. This phase confirmed the dose dependant deterioration in SDLP, with the lower doses producing impairment less than 0.05g/100mL and the highest dose producing impairment marginally above that. The subjects rated their performance as worse than normal at the two highest doses, but still expressed a willingness to drive.

The final phase of the study involved more demanding urban city driving, and consequently only the placebo and lowest dose were administered since the prior two phases had shown significant impairment in the two highest dose conditions. In this phase the drivers performance was compared against other drivers dosed to a 0.05g/100mL BAC. The alcohol condition produced the expected deterioration in driving performance, but the 100ug/Kg THC dose produced no measurable decline in urban city driving performance. Interestingly the alcohol impaired drivers reported no perceived deterioration in performance even while it was evident to the observers, while conversely the subjects receiving the low dose THC reported feeling impaired even while no impairment could be measured. This echoes the experience of Klonoff's study that users were compensating, and often overcompensating for their perceived impairment.

Most importantly, this careful work demonstrates that while marijuana has the ability to impair, under certain conditions, and does so in a dose dependant manner, the degree of impairment associated with a user preferred dose of 300 ug/Kg, produced impairment equivalent to BACs of 0.03 - 0.07 g/100 mL. Additionally it confirmed the lack of correlation between plasma THC concentrations and the level of impairment.

Lamers and Ramaekers, 2001

In this study, performed at the same institute and using the same methodology, researchers assessed the combined effects of alcohol and marijuana using 0.04g/100mL BAC and 100ug/Kg THC on urban city driving. Additionally, using a head mounted eye movement recording system the subjects' visual search or side glances were assessed.

This study confirmed that low doses of marijuana, or alcohol at the 0.04g/100mL concentration, when taken alone, did not impair city driving, performance or interfere with visual search frequency at intersections. When alcohol and THC were taken in combination however, visual search frequency decreased by about 3%. The study also confirmed the finding of previous work that subjects did not feel impaired when using alcohol, even when impairment was present, but did feel impaired after marijuana use even when no impairment was measurable. Subjects' ability to recognize their impairment from marijuana was abolished however, when it was consumed in conjunction with alcohol.

Conclusions

The material reviewed in this chapter highlight the challenges of assessing driving impairment caused by marijuana. Epidemiologically, there is evidence for dose dependant increases in crash risk with increasing blood THC concentration. There is good evidence that the prevalence of cannabinoids in the system of injured, killed and arrested drivers is higher than the incidence in the population at large. Empirically the drug produces effects on cognition and psychomotor performance which have the potential to impair driving ability, and users recognize the presence of that impairment and can even compensate accordingly. There is good evidence that there is a significant dose response relationship between marijuana use and the degree of impairing effects. On the other hand, the passage of time between driving or involvement in a crash limits our ability to get an accurate measurement of the THC concentration at the time of driving. More complex tasks are more sensitive to the effects of marijuana, and increase the likelihood that that the impairment will become significant and observable.

Studies of driving behavior have been conducted with typical user-preferred doses, and show that the effects, at least on the alcohol impairment scale, are mild to moderate, and are affected by the dose, the time since use, the users' perception of the effect, and their degree of compensation or overcompensation for those effects.

In short, the assessment of the role of marijuana use in a crash or impaired driving case must be made with caution, and will be most defensible when all available information is considered, including the pattern of driving, recent drug use history or admission to marijuana use, an appearance of impairment, performance in field sobriety tests, the presence of physiological signs and symptoms of marijuana use, and toxicological test results of blood or serum samples.

General Reading

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